Disability-Adjusted Life Year Estimation: HIV Pilot Study

METHODOLOGY & RESULTS

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AIM

We have previously conducted multiple validation studies of our online disability-adjusted life year (DALY) calculator to replicate DALY estimates from published studies. The aim of the current study is to pilot test methods for estimating DALYs, DALYs averted, and cost per DALY averted in a sample of studies that have exclusively used cost per case averted as the primary measure of cost-effectiveness.

METHODS

STUDY SELECTION

We searched published, English-language systematic reviews of studies of the effectiveness and cost-effectiveness of interventions for individuals with or at risk of HIV. Candidate studies were considered from these reviews if they reported cases averted; we included both program evaluations and modeling studies. We excluded reviews, editorials, and purely methodological articles. Studies were not restricted by setting, intervention, or population. A total of 25 studies were selected for the pilot, published between 1994 and 2019. These studies are summarized in Table 1.

DATA EXTRACTION

We extracted information on study methods and results including study country, intervention, comparator, target population characteristics (i.e., gender, age, and population size), discount rate, cases averted, incremental costs, cases averted, and gross domestic product (GDP) per capita. Based on the study country and target population characteristics, we obtained case fatality estimates from the 2017 GBD study[1] to calculate the number of deaths averted.

ONLINE CALCULATOR

The online DALY calculator is a Web app that, on individual and population levels estimates years of life lost (YLL), years lived with disease (YLD), and total DALYs attributable to a particular disease. Further details regarding the DALY calculator are published elsewhere.[2] The online DALY calculator includes disability weights and life expectancy at death that are fixed parameters pulled from standardized data sources[3-5] depending on disease, country, gender and age of death input by a user.

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Our application of the DALY calculator in this instance focused on individual-level calculations, given the primary interest in estimating the number of DALYs that would be saved by averting each case of HIV, dependent on geographic setting and the characteristics of the target population. Importantly, we used an incidence-based approach to estimating YLD rather than the more recent prevalence-based approach published by the GBD, given the individual-level calculations of interest.

Data analysis

We conducted probabilistic analyses to reflect the uncertainty in the following input parameters: age of HIV onset, duration of each disease stage, disability weight for each disease stage, and life expectancy as of the age of onset. We calculated the mean age of HIV onset based on the age range of the target population. We further assumed that age at disease onset would follow a gamma distribution since it is a continuous non-zero value. The mean and standard error for duration and disability weight of each HIV stage, and life expectancy at age of onset were sourced externally.[4-6] We adjusted the duration estimates from this study to reflect the age, gender, and country- specific life expectancy. Based on the distribution characteristics of each probabilistic input parameter (i.e., dispersion, skewness, and kurtosis), we assume that duration of each HIV stage follows a gamma distribution, disability weight of each HIV stage follows a beta distribution, and life expectancy at age of onset follows a normal distribution.

We then used Monte Carlo simulation to integrate the uncertainty from input parameters over 1,000 iterations without replacement for each study-specific set of estimates. We report the mean DALYs per HIV case estimated for each study, along with a "bootstrapped" uncertainty interval (i.e., using the 2.5% and 97.5% percentiles of the differences between each simulation and the overall simulation mean for YLL, YLD and DALY estimates respectively). Based on reported incremental costs, we also estimated the cost-per-DALY averted using the calculated mean DALYs from the simulation. This was presented both in terms of the costs reported in USD for the given study and with these costs updated to 2019 USD using relevant currency exchange rates and the medical care component of consumer price index (https://www.bls.gov/cpi/). The latter was compared to current country-specific estimates of GDP per capita as a benchmark of potential cost-effectiveness.

Table 2 presents the results from all 25 studies in our sample. We also compared our estimates of DALYs to those reported in two studies from our sample that provided estimates of both DALYs and cases averted. The first study from Kahn et al. [7] studied the cost-effectiveness of adult male circumcision for HIV prevention in South Africa. This study estimated 14.95 DALYs averted per HIV infection, largely as a result of a straightforward average of the DALYs per case of untreated vs. treated HIV without a link to remaining life expectancy in a South African setting. Our model generates a higher estimate of 21.23 (UI 15.08-37.42, see Table 2) DALYs based on our assumption of multiple stages of HIV (i.e., including asymptomatic and symptomatic but untreated) as well as a direct link to South African life expectancy estimates. Estimates for the other study (Fasawe et al.[8]) of prevention of pediatric HIV in Malawi totaled 22.50 DALYs averted per HIV case, but no details were provided on the derivation of the estimate; our result was higher (27.27 [24.22-32.11], see Table 2), likely due again to a more precise estimate of age of death based on time spent in each stage of HIV.

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Table 1. Study Summary

Author (year)	*Country*	*Target population*	*Intervention*	*Comparator*
Awad (2015)	Zimbabwe	1,625,000 males aged 13-29	VMMC 2010-2025	No circumcision
Binagwaho (2010)	Rwanda	150,000 adults aged 30	VMMC 2010-2026	No circumcision
Cohen (2006)	United States	275,000 female adults age 13-64	Condom availability/accessibility	Lifetime HIV treatment
Cremin (2015)	Mozambique	2,650,000 18+ adults	Time-limited PrEP for partners of migrant miners	PrEP all year
Cremin (2015)	Kenya	2.65 million population 15-49 in Nyanza province	PrEP 2015-2025	None
Dugdale (2019)	South Africa	3.1 million women with HIV (aged 15 to 49 years) starting or continuing first-line ART, and their children	Dolutegravir for all women of child-bearing potential (DTG)	Efavirenz for all women of child-bearing potential (EFV)
Fasawe (2013)	Malawi	66,500 HIV-infected 18-59 year-old pregnant women	Lifelong ART for HIV+ women	Current practice: HIV testing + counselling and ARV prophylaxis
Fung (2007)	India	4,000 females aged 33	Outreach, peer education, condom distribution, and free STD clinics for sex workers	None
Hausler (2006)	South Africa	296,000 females aged 15-49	Voluntary counselling and testing	None
Juusola (2011)	United States	6,435,210 males aged 13-64	Antibody + viral load testing + symptom-based screening for HIV infection in men who have sex with men	Status quo
Kahn (2006)	South Africa	1,000 males aged 18+	1,000 circumcisions over 20 years	No circumcision
Kripke (2016)	Zimbabwe	1,300,000 males aged 20-29	VMMC 2015-2029	Usual care
Kripke (2016)	Swaziland	144,688 HIV-negative males aged 15-24	VMMC 2014-2048	Usual care
Kripke (2016)	Malawi	9,291,984 males aged 15-49	VMMC 2014-2048	Baseline VMMC levels
Kripke (2016)	South Africa	18,551,891 males aged 15-49	VMMC 2014-2048	Baseline VMMC levels

Author (year)	Country	Target population	Intervention	Comparator
Kripke (2016)	Tanzania	17,967,487 males aged 15-49	VMMC 2014-2048	Baseline VMMC levels
Kripke (2016)	Uganda	26,391,854 males aged 15-49	VMMC 2014-2048	Baseline VMMC levels
Long (2014)	UK	93,400 adults aged 15-64	High-risk testing every 1 year, low-risk testing one time + ART	Status quo
Lurie (1994)	United States	31,146,000 adults aged 15-54	Voluntary counseling and inpatient testing to avert health care worker infections for 1 year	Status quo
Menon (2014)	Tanzania	Males aged 15-49	VMMC 2016-2025	No scale up VMMC program
Nakakeeto (2009)	Multiple	Adults aged 15-49	HIV+ family planning, HIV testing/counseling in pregnancy, prophylaxis to HIV-infected women and exposed infants	Not stated
Njeuhmeli (2016)	Zimbabwe	9 million infants and males aged 10-34	Early infant male circumcision (EIMC)+Voluntary medical male circumcision (VMMC)	VMMC program
Njeuhmeli (2011)	Botswana	1,080,000 population aged 15-49	VMMC 2011-2025	No expanded circumcision program
Njeuhmeli (2011)	Malawi	6,840,000 population aged 15-49	VMMC 2011-2027	No expanded circumcision program
Njeuhmeli (2011)	Mozambique	10,300,000 population aged 15-49	VMMC 2011-2028	No expanded circumcision program
Njeuhmeli (2011)	Namibia	1,090,000 population aged 15-49	VMMC 2011-2029	No expanded circumcision program
Njeuhmeli (2011)	Kenya	1,510,000 population aged 15-49	VMMC 2011-2030	No expanded circumcision program
Njeuhmeli (2011)	Rwanda	4,490,000 population aged 15-49	VMMC 2011-2031	No expanded circumcision program
Njeuhmeli (2011)	South Africa	26,800,000 population aged 15-49	VMMC 2011-2032	No expanded circumcision program
Njeuhmeli (2011)	Swaziland	590,000 population aged 15-49	VMMC 2011-2033	No expanded circumcision program
Njeuhmeli (2011)	Tanzania	19,600,000 population aged 15-49	VMMC 2011-2034	No expanded circumcision program

Author (year)	*Country*	*Target population*	*Intervention*	*Comparator*
Njeuhmeli (2011)	Uganda	14,100,000 population aged 15-49	VMMC 2011-2035	No expanded circumcision program
Njeuhmeli (2011)	Zambia	6,850,000 population aged 15-49	VMMC 2011-2036	No expanded circumcision program
Njeuhmeli (2011)	Zimbabwe	6,190,000 population aged 15-49	VMMC 2011-2037	No expanded circumcision program
Rutstein (2013)	Malawi	5,000 adults aged 15-49	Provider notification (provider attempts to notify indexes' locatable partners)	Standard of care: passive referral (index is encouraged to notify partners)
Teerawattananon (2005)	Thailand	1 million pregnant women	2 sessions voluntary counseling with ART	Usual care
Walensky (2016)	South Africa	1 million high-risk South African women with a mean age (SD) 18 (2) years	Novel long-acting formulas of pre-exposure prophylaxis (LA-PrEP)	No PrEP
White (2008)	Zambia	53,337 population aged 15-49	Syndromic STI case management	Lifetime HIV treatment
White (2008)	Kenya	50,846 population aged 15-49	Syndromic STI case management	Lifetime HIV treatment
White (2008)	Benin	72,334 population aged 15-49	Syndromic STI case management	Lifetime HIV treatment
White (2008)	Cameroon	68,244 population aged 15-49	Syndromic STI case management	Lifetime HIV treatment
Ying (2016)	South Africa	Population aged 0-59	Home testing and counselling + expanding ART eligibility to people with a CD4 count >350 cells per µL and a viral load >10,000	Initiation of treatment for those who have viral loads >10,000 copies per mL

Table 2. Results

Author (year)	*Country*	*Cases averted*	*Incremental costs per person*	*Original ICER ($/case averted)*	*DALYs per HIV Case (95% UI)*	*Calculated ICER ($/DALY)*	*Updated ICER (2019) ($/DALY)*	*GDP Benchmark (2019)*
Awad (2015)	Zimbabwe	314,000	196	1,025	19.53 (11.79-25.53)	$278	$332	<1xGDP per capita
Binagwaho (2010)	Rwanda	859	34	5,877	18.84 (13.28-27.17)	$224	$310	<1xGDP per capita
Cohen (2006)	United States	136	6	22,000	18.52 (7.64-33.10)	$3,621	$5,985	<1xGDP per capita
Cremin (2015)	Mozambique	49,450	49	2,621	18.05 (9.78-30.11)	$3,469	$4,142	>3xGDP per capita
Cremin (2015)	Kenya	49,450	38	2,060	18.55 (9.81-31.02)	$633	$756	<1xGDP per capita
Dugale (2019)	South Africa	45,667	NA	NA	18.64 (10.69-32.70)	NA	NA	Cost-saving
Fasawe (2013)	Malawi	15,997	1,255	1,265	27.27 (24.22-32.11)	$260	$339	<1xGDP per capita
Fung (2007)	India	5,755	115	80	17.50 (12.51-24.98)	$21	$33	<1xGDP per capita
Hausler (2006)	South Africa	29,600	10	97	12.08 (8.68-19.57)	$35	$60	<1xGDP per capita
Juusola (2011)	United States	38,995	2,528	417,209	17.31 (5.89-30.37)	$133,917	$179,973	>3xGDP per capita
Kahn (2006)	South Africa	308	Cost saving	Cost saving	21.23 (15.08-37.42)	Cost saving	Cost saving	Cost saving
Kripke (2016)	Zimbabwe	63,000	341	7,035	18.36 (13.04-24.92)	$2,753	$3,592	1-3xGDP per capita
Kripke (2016)	Swaziland	20,000	224	1,620	21.54 (17.04-26.81)	$589	$683	<1xGDP per capita

Author (year)	Country	Cases averted	Incremental costs per person	Original ICER ($/case averted)	DALYs per HIV Case (95% UI)	Calculated ICER ($/DALY)	Updated ICER (2019) ($/DALY)	GDP Benchmark (2019)
Kripke (2016)	Malawi	149,000	80	4,968	16.77 (6.66-24.42)	$1,772	$2,054	>3xGDP per capita
Kripke (2016)	South Africa	375,000	59	2,916	17.42 (6.64-24.54)	$1,015	$1,177	<1xGDP per capita
Kripke (2016)	Tanzania	53,400	19	6,264	16.90 (6.89-25.22)	$2,031	$2,354	1-3xGDP per capita
Kripke (2016)	Uganda	486,000	30	1,620	16.64 (6.66-25.16)	$553	$641	<1xGDP per capita
Long (2014)	United Kingdom	4,920	66	1,252	18.92 (8.68-31.72)	$404	$497	<1xGDP per capita
Lurie (1994)	United States	4	159	1,372,129,159	19.96 (10.62-33.29)	$358,010,468	$795,244,716	>3xGDP per capita
Menon (2014)	Tanzania	167,500	NA	3,752	17.15 (7.61-29.13)	$25,121	$32,777	>3xGDP per capita
Nakakeeto (2009)	Multiple	486,625	NA	1,584	17.07 (14.68-18.21)	$589	$840	<1xGDP per capita
Njeuhmeli (2016)	Zimbabwe	266,000	747	2,808	19.37 (12.27-29.92)	$221	$256	<1xGDP per capita
Njeuhmeli (2011)	Botswana	60,000	Cost saving	Cost saving	18.98 (10.34-31.83)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Malawi	240,000	Cost saving	Cost saving	18.44 (10.12-30.42)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Mozambique	220,000	Cost saving	Cost saving	17.94 (9.78-29.33)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Namibia	20,000	Cost saving	Cost saving	19.10 (10.51-31.34)	Cost saving	Cost saving	Cost saving

Author (year)	*Country*	*Cases averted*	*Incremental costs per person*	*Original ICER ($/case averted)*	*DALYs per HIV Case (95% UI)*	*Calculated ICER ($/DALY)*	*Updated ICER (2019) ($/DALY)*	*GDP Benchmark (2019)*
Njeuhmeli (2011)	Kenya	70,000	Cost saving	Cost saving	18.66 (10.01-30.70)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Rwanda	60,000	Cost saving	Cost saving	18.47 (9.39-31.04)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	South Africa	1,080,000	Cost saving	Cost saving	19.42 (11.45-32.26)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Swaziland	60,000	Cost saving	Cost saving	17.83 (9.68-30.04)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Tanzania	200,000	Cost saving	Cost saving	18.58 (9.28-31.32)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Uganda	340,000	Cost saving	Cost saving	18.25 (9.23-30.74)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Zambia	340,000	Cost saving	Cost saving	18.35 (9.53-30.66)	Cost saving	Cost saving	Cost saving
Njeuhmeli (2011)	Zimbabwe	570,000	Cost saving	Cost saving	17.91 (9.05-29.83)	Cost saving	Cost saving	Cost saving
Rustein (2013)	Malawi	28	27	4,814	18.99 (10.94-31.45)	$1,751	$2,285	>3xGDP per capita
Teerawattananon (2005)	Thailand	353	6	1,759	21.16 (18.48-23.75)	$470	$754	<1xGDP per capita
Walensky (2016)	South Africa	156,000	870	5,577	23.77 (20.37-29.31)	$36,593	$42,421	>3xGDP per capita
White (2008)	Zambia	220	2	463	18.00 (9.03-30.24)	$160	$272	<1xGDP per capita
White (2008)	Kenya	28	1	2,164	18.47 (9.88-31.47)	$636	$1,083	<1xGDP per capita

Author (year)	*Country*	*Cases averted*	*Incremental costs per person*	*Original ICER ($/case averted)*	*DALYs per HIV Case (95% UI)*	*Calculated ICER ($/DALY)*	*Updated ICER (2019) ($/DALY)*	*GDP Benchmark (2019)*
White (2008)	Benin	6	1	7,183	18.31 (8.87-30.93)	$2,075	$3,533	1-3xGDP per capita
White (2008)	Cameroon	49	2	2,404	18.16 (8.97-30.47)	$727	$1,238	<1xGDP per capita
Ying (2016)	South Africa	43,000	NA	3,153	21.69 (14.13-37.27)	$1,035	$1,131	<1xGDP per capita